BACKGROUND

XmAb®20717 is a bispecific antibody, with a mouse IgG1 Fc domain, that targets programmed death-1 (PD-1) and CD155, encoded by the tumor growth factor-β (TGF-β)-related protein β2 (Tbet). The β2, a member of the TGF-β superfamily, is upregulated in multiple cancer subtypes. XmAb®20717 preferentially engages Tbet-expressing tumor cells in the absence of profound off-target effects.

Methods

We conducted a randomized, open-label, Phase 1 clinical trial, examining XmAb®20717, in patients with locally advanced or metastatic NSCLC (NCT03005303). Patients were randomized to receive XmAb®20717 at one of four dose levels: 0.1, 0.3, 1, or 3 mg/kg. Treatment cycles consisted of two weekly infusions of XmAb®20717 followed by a 21-day rest period. Primary outcome measures included preliminary antitumor activity and safety, and preliminary pharmacokinetics/pharmacodynamics.

RESULTS

Thirty-two patients received at least one dose of XmAb®20717 (0.1 mg/kg, n=3; 0.3 mg/kg, n=8; 1 mg/kg, n=11; and 3 mg/kg, n=10). Fourteen patients (44%) achieved a response (confirmed partial response, n=5; confirmed complete response, n=9). The estimated 30-day and 60-day treatment-related adverse event rates were 82% and 94%, respectively. The most frequent treatment-related adverse events were fatigue (78%), nausea (63%), dyspnea (53%), anorexia (50%), and nausea (44%). There were no treatment-related deaths.

CONCLUSIONS

XmAb®20717 was generally well-tolerated. The most common treatment-related adverse events were generally manageable and consistent with the expected immune-related toxicities of this class of immune checkpoint inhibitor antibody. Further study in patients with NSCLC is recommended, given the high response rate observed in this study.

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